

REMARKS

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Claims 1, 36, 39, 56, and 57 are pending in the present application. Claims 51-55 have been cancelled as being drawn to a nonelected invention. Claims 2 - 4 have also been cancelled. Claims 1, 36, and 39 have been amended, and new claims 56 and 57 have been added. The amendments to claims 1, 36, and 39 are supported by the claims as originally filed. New claim 56 is supported by disclosure at page 106, lines 9-22 of the specification. New claim 57 is supported by disclosure at page 98, lines 21-29 and at page 10, lines 6-7 of the specification. No new matter has been added.

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SPECIFICATION

The Examiner has objected to the specification because it contains embedded hyperlinks and/or other forms of browser-executable code. In accordance with the Examiner's instructions and MPEP § 608.01, Applicants have amended the specification to remove the hyperlinks and browser-executable code.

CLAIM REJECTIONS

The §112, second paragraph rejections

Claims 1-4, 36 and 39 have been rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness. Specifically, the Examiner states that claim 1 is unclear because it recites "a mature form" and because it recites "variant". Claim 1 has been amended to delete the phrases "a mature form" and "variant", and to recite an isolated polypeptide comprising an amino acid sequence of SEQ ID NO: 4. Therefore, claim 1 no longer recites "a mature form" or "variant". Thus, Applicants contend that claim 1 and the claims that depend therefrom, as amended, are clear and definite.

According to the Examiner, claim 4 is unclear because it recites "a conservative amino acid substitution". Claims 2 - 4 have been cancelled. Therefore, the rejection, as it applies to these claims, is moot.

For the reasons discussed above, Applicants assert that this rejection should be withdrawn.

The § 112, first paragraph rejections

Claims 1-4, 36 and 39 have been rejected under 35 U.S.C. § 112, first paragraph for lack of written description. According to the Examiner, the claims are drawn to a genus of proteins related to SEQ ID NO: 4, which includes a large number of unpredictable species. The Examiner states that the specification provides evidence for only a single species of SEQ ID NO: 4. Claim 1 has been amended to recite an amino acid sequence of SEQ ID NO: 4. The amino acid sequence of SEQ ID NO: 4 is disclosed at page 10, Table 1D of the specification. Therefore, Applicants contend that the subject matter of claim 1, and that of the claims that depend therefrom, is adequately described by the instant specification. Claims 2 - 4 have been cancelled. Thus, this rejection should be withdrawn.

To the extent that this rejection is applied to new claim 56, Applicants assert that the specification provides written description for polypeptides that are at least about 95% homologous to SEQ ID NO: 4. *See* specification at page 106, lines 9 - 22. Likewise, for new claim 57, Applicants contend that the specification identifies the signal peptide cleavage site between residues 38 and 39 of SEQ ID NO: 4. *See* specification at page 10, lines 6 - 7. Such proteolytic cleavage of a signal peptide results in a mature form of a polypeptide, as described in the specification. *See* specification at page 98, lines 21 - 23. Therefore, new claims 56 and 57 meet the written description requirement of 35 U.S.C. § 112, first paragraph.

The § 101 rejections

Claims 1-4, 36 and 39 have been rejected under 35 U.S.C. § 101 as lacking support by a credible, specific and substantial asserted utility or a well-established utility.

The Examiner states that the application does not teach a relationship to any specific disease or establish any involvement of the claimed invention in the etiology of any specific disease or does not teach the function(s) of the protein. Further, the Examiner asserts that the claimed polypeptide is not shown to be overexpressed or underexpressed in a specific diseased tissue compared to healthy tissue. The Examiner reasons that the proposed use of the claims are starting points for further investigation. Therefore, Examiner concludes that the specification

does not support a credible, specific and substantial utility because the specification does not provide guidance as to how one of skill in the art could use the claimed invention. Applicants traverse.

Applicants submit that at least one substantial and specific utility exists for the claimed invention and is readily apparent based on the teachings of the specification, *e.g.*, at page 22, line 15 through page 23, line 7 and at page 141, line 32 through page 142, line 15. In addition to the disclosed utilities, which the Examiner has keenly ascertained to be described throughout various locations in the specification, Applicants respectfully assert that the claimed protein, SEQ ID NO:4, is useful, *inter alia*, as a marker (prognostic indicator) for cancer. Specifically, SEQ ID NO: 4 can be used in the diagnosis of lung, breast, ovarian, and bladder cancer, thereby demonstrating a “real world” use and patentable utility (*See*, the C.F.R. § 1.132 declaration of Dr. Valerie Gerlach, “Gerlach Declaration”, attached hereto).

The expression of SEQ ID NO:4 is dynamically modulated and/or aberrantly expressed in cancer cell lines. In the Gerlach Declaration, included herewith, Tables 3-5 depict the scaled results of quantitative gene expression analyses. Gene-specific primers were used to measure the relative SEQ ID NO:4 expression levels in normal cells or tissues, stimulated cells, or pathological tissue samples. The Relative Expression Score for each sample indicates the relative quantity of a SEQ ID NO:4 transcript, with 0.0 indicating no detectable expression and 100.00 indicating highest detectable expression level.

In the Gerlach Declaration attached, Dr. Valerie Gerlach states that SEQ ID NO:4 is expressed in various tissues of a comprehensive panel, but a significant expression level is observed in breast cancer cell lines, ovarian cancer cell lines and lung cancer cell lines when compared to their controls. (*See* Table 3, Panel 1.3D).

In another panel (*see* Table 4, Panel 2D), the difference in expression of SEQ ID NO: 4 is shown between samples derived from human cancer tissue and “matched margins” obtained from noncancerous tissue adjacent to the tumor. These results demonstrate that SEQ ID NO:4 is proximally linked to cancer cell physiology and pathophysiological events, particularly in breast, bladder or ovarian cancer. This gene or gene product was also observed to be expressed at low levels in various cultured human cell lines confirming the results obtained in Table 4.

Applicants assert that the specification identifies and the accompanying C.F.R. § 1.132 declaration supports at least one specific and credible utility. The invention as claimed is useful as a marker for identifying cancer cells. Thus, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §101.

To the extent that this rejection is applied to new claims 56 and 57, Applicants assert that the invention, as claimed therein, is also useful as a marker for identifying cancer cells. Thus, Applicants contend that new claims 56 and 57 meet the utility requirement of 35 U.S.C. §101.

The § 112, first paragraph rejections

Utility-Based Rejections

Claims 1-4, 36 and 39 have been rejected under 35 U.S.C. § 112, first paragraph because one skilled in the art would not know how to use the invention since the claimed invention lacks utility. As discussed above, throughout the specification, and attested to by 1.132 affidavit, claims 1, 36, 39, and new claims 56 and 57, have a specific, substantial, and credible utility. Claims 2 - 4 have been cancelled. Therefore, Applicants submit that this rejection should be withdrawn.

The § 102, first paragraph rejections

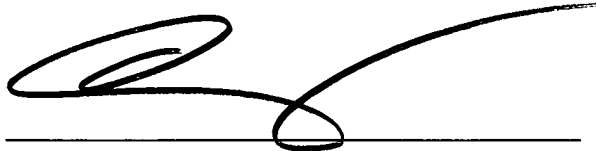
Claims 1-4, 36, and 39 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Rouquier *et al.*, Nat. Genet., 18:243-50 (1998). According to the Examiner, Rouquier *et al.* teach a polypeptide, which has 68.3% identity to SEQ ID NO: 4. Claim 1 has been amended to recite an amino acid sequence comprising SEQ ID NO: 4. The overall sequence of the polypeptide of Rouquier *et al.* differs by 31.7% from the polypeptide sequence of SEQ ID NO: 4. Therefore the polypeptide of Rouquier *et al.* does not disclose all of the elements of the claimed invention. Thus, the reference does not anticipate the claims, as amended herein, and this rejection should be withdrawn.

To the extent that this rejection is applied to new claims 56 and 57, Applicants contend that the polypeptide taught by Rouquier *et al.* differs significantly from the polypeptides of new claims 56 and 57. Therefore, the reference does not anticipate claims 56 and 57.

CONCLUSION

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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